





THE ANNUAL ORATION.—“THE CAUSE OF THE HEART-BEAT.”

By G. A. GIBSON, M.D., D.Sc., LL.D.

ON glancing over the Orations of the Medical Society for the last twenty years, it is clear that most of the previous occupants of the distinguished position to which your generous kindness has called me have occupied themselves with matters, whether of wide general interest or more restricted application, to which they have given particular attention. Following in the path chosen by my predecessors, the best mode of showing my appreciation of the honour which you have done me will certainly consist in devoting my remarks, with your permission, to some subject with which I am more specially conversant.

Time and again, the mind of man has in the past appeared to reach the end of fruitful endeavour. Knowledge has been accumulated and facts have been gathered until a stage has been reached when further advance has appeared to be impossible. This was the case with several epochs during last century; observers looked back with amazement at the strides which had taken place, and shrunk from looking forward, in despair of being able to add anything to the general store. Yet, when considering these particular times at a later period, it has been clear that during them mankind has been blind to the riches of nature lying ready for research. Nowhere is this better expressed than by the distinguished Sir Isaac Newton. “I seem,” he says, “to have been only like a boy playing on the seashore and diverting myself in now and then finding a smoother pebble or a prettier shell than ordinary, whilst the great Ocean of Truth lay all undiscovered before me.” The reflection is one well calculated to cheer us in any mood of despondency, as showing the possibility for each and all of us in our several spheres to contribute something to modern science. In this connection, one of the beautiful legends of antiquity inevitably rises before the memory. You remember how Philemon and Baucis were sitting at their door after the evening meal, when two travellers, who had been refused shelter at the

hands of the neighbouring villagers, approached the cottage. The worthy couple courteously invited the travellers to enter their abode, and set before them of their best. To the sorrow of Baucis, however, their store was scanty, and one or two deep draughts exhausted the milk contained in the pitcher. At the magic touch, however, of the staff which was carried by the younger of the two travellers, the vessel became endowed with inexhaustible properties. Little wonder that it was so, for the two travellers were Zeus and Hermes. Nature is, indeed, like the pitcher of Baucis—when approached by the right person she yields an unending supply.

In the domain of the circulation, remarkable strides have been made within the last few years, not only in the clinical study of its disturbances, but also in the pathological observation of its structural changes, the physiological investigation of its normal phenomena, and even the anatomical elucidation of its morphological features. In all these different branches of study numerous new facts have been brought to light, and much of our knowledge has been literally recast. Unfortunately, the interpretation of the facts is not always such as will satisfy the inquiring mind.

It may savour of temerity to enter upon the discussion of such a thorny subject as that selected for this evening. Not only does it abound with inherent difficulties of no ordinary kind, but these have been rendered more serious by the warmth which has too often entered into the discussion of the subject. It has, indeed, formed one of the battlefields of modern science. Doughty champions have entered the lists in defence of views which they have been led to espouse, and in one or two quarters the discussions which have arisen have been, to put it mildly, somewhat acrimonious. To my own mind it has been a subject of regret that certain of the protagonists seem to have regarded the views which they hold as little short of infallible dogmas, and have emulated the fervour of the Churchmen—no disrespect is implied in this remark—rather than the inquiring spirit of the man of science. In the quest of truth, it is our bounden duty to be in earnest. “*Felix qui quod amat defendere fortiter audet*” is an admirable motto; there are, however, ways of upholding what we know to be true and of defending what we feel to be right, without sinking into unseemly wrangles. “A good cause,” says Sir Thomas

Browne, "needs not to be patroned by passion, but can sustain itself upon a temperate dispute." In the attempt which is now about to be made to ascertain the facts in regard to one of the much debated problems of the present age, it will be my duty to avoid anything savouring of partisanship, and to remain free from heat in the discussion of the arguments. My sole aim will be to make an honest effort to attain as nearly as possible to the real cause of the appearances under review, remembering the wise remark of Carlyle: "Truth of any kind breeds ever new and better truth."

The literature which has already grown up in connection with the subject is enormous. It is quite impossible, in the compass of a single lecture, to do more than refer to the really important contributions yielding something more than mere destructive criticism. For an excellent summary of the whole question of the cause of the heart-beat, let me refer to the learned article of Langendorff in the "*Ergebnisse der Physiologie*," and allow me further to add that, while this oration was in course of preparation, two interesting addresses have appeared on the subject by Wesley Mills and Alexander Morison.

Harvey made no attempt, even in that chapter which forms the most beautiful part of his immortal work, to explain the causes of the pulsation of the heart, and we have to pass on till a period 130 years later before we encounter any attempt to define the problem. Cardiac movements were originally attributed by Albrecht von Haller to an inherent power of contraction belonging to the heart itself. It has been claimed that he regarded the automatic movements of the heart as due to an inherent faculty of the heart muscle. This, however, is not specifically stated, and, as the intimate nervous connections were then unknown, it is probable that the intrinsic nature of the movements did not particularly trouble the mind of that great observer. Senac also regarded the pulsation of the heart as due to special cardiac activities, but he at the same time laid greater stress upon external sources of interference. With these vague views, pathologists as well as physicians were content until the middle of last century. The discovery of the ganglia at the junction of the sinus and auricle by Remak, of those between the auricle and ventricle by Bidde, and of those between the two ventricles by Ludwig, necessarily opened up the possibility

of some definite explanation, and the formal presentation of the views which resulted was given by Volkmann, who enunciated the theory that the pulsation of the heart was due to the automatic action of its intrinsic ganglia.

These views, however, were modified in certain respects, from time to time, by the investigations of several observers. It is only necessary to mention the experiments of Eekhard, as well as of Foster and Dew Smith, upon the apical region of the heart, and the further researches of Bowditch and of Merunowicz on the influence of different nutrient fluids upon the same cardiac region, to show that modifications of the explanation went on. The general result of these different investigations, however, was embodied in the theory stated by Rosenthal, that impulses flowed from the ganglia in the sinus and produced the rhythmic action of the heart.

In the minds of those, nevertheless, most competent to form a judgment in respect of the facts, a considerable degree of doubt existed in regard to their explanation. This cannot be better proved than by referring to the remark of Foster, in the first edition of his "Text-book of Physiology," which appeared two years after Rosenthal's statement; this we may take to be a landmark or guide to the state of knowledge of the epoch in which it appeared. "In the sporadic ganglia," Foster says, "the evidence of automatic action seems more clear, and yet is by no means absolutely decisive. The beat of the heart is a typical automatic action: and, since the heart will continue to beat for some time when isolated from the rest of the body (that of a cold-blooded animal continuing to beat for hours, or even days), its automatism must lie in its own structures. When, however, we come to discuss the beat of the heart in detail, we shall find that it is still an open question whether the automatism is confined to the ganglia (either of the sinus venosus, auricles, or auriculo-ventricular boundary), or shared in by the muscular tissue: whether, in fact, the automatism is a muscular automatism like that of a ciliated cell, or the automatism of a differentiated nerve cell. And yet the heart is the case where the automatism of the ganglia seems clearest."

At this point we reach the parting of the ways.

The long series of researches made by Gaskell and embodied in a valuable paper, which has for well nigh a quarter of a century

been a constant subject of study amongst all of us interested in the problems of the circulation, may be regarded as the starting-point of the myogenetic theory. In this admirable contribution the author enunciates two laws, as follows: "The power of independent rhythmical contraction decreases regularly as we pass from the sinus to the ventricle," so runs the first law; the second is—"the rhythmical power of each segment of the heart varies inversely as its distance from the sinus." These conclusions have never been controverted, and from an exoteric point of view there is practically unanimity regarding them. It is when we approach their esoteric consideration that we are struck by the fact, and it is a somewhat important fact, that the phenomena are susceptible of explanation in two absolutely antagonistic ways. Going on to examine the rhythm of the heart and the contraction of its walls by the study of movements in strips of muscle, Gaskell concludes that the contractions are myogenetic and automatic. He bases his belief in the myogenetic origin of the contractions on the absence of special nerve structures, and on the fact that when the rhythm is once well established the strip can be cut into small pieces, each of which will still continue its rhythm for a long time. The origin of the movements must, therefore, according to Gaskell, be either in the muscle cells or nerve fibres, as was suggested by Schiff in discussing the movements of the heart. It is to be noted in passing that Gaskell does not deny nerve influence. By the method of its development Gaskell was led to the conclusion that the rhythm is due to some quality inherent in the muscle itself, *i.e.*, that it is automatic. He holds that nothing can be more striking than the nature of its development, the gradual recovery of conduction, the steady increase of the contraction, the uniform augmentation of excitability—all show a steady improvement in the activity of the processes upon which the various properties of the muscle depend, which is manifested by the outburst of automatic rhythmical contractions. It continues for many hours after the discontinuance of all stimulation. Gaskell shows that the ventricle contracts in due sequence with the auricle, and shows by experiment that this occurs only when a contraction wave passes to the groove. He points out the special structure of the muscular fibres at the sino-auricular junction, forming a regular band or muscular ring from which the fibres of the auricle take their origin; and again at the auriculo-ventricular junction, where

there is another well-defined ring of parallel muscular fibres, from which, in part, the muscular fibres of the ventricle take their origin. The existence of these two muscular rings connecting the two muscular cavities of the heart is, according to Gaskell, amply sufficient to account for the passage of the contraction from the sinus to the auricle, and from the auricle to the ventricle, without the necessity of invoking the presence of ganglion cells. He next repeats the experiments of Eckhard and Marchand, which led them to conclude that the auriculo-ventricular ganglia are essential for the due sequence of the ventricular upon the auricular contractions in the frog, and he asserts that, after removing them, the sequence continues just as well as before. From a few observations upon the heart of the skate, he concludes that it affords a good example of the peristaltic nature of the heart-beat, and also furnishes a new proof that the starting-point of the peristaltic contractions is determined by the nature of the muscular substance, rather than by the presence or absence of ganglion cells.

Gaskell proves that the cardiac nerves are able to increase and diminish the conductivity of the muscular tissue of the auricle, and he points out that the refractory phase discovered by Marey is applicable to any portion of cardiac muscle along which a contraction wave passes, so that a certain time must elapse after every wave before conductivity is sufficiently restored to permit another to travel. The effect of injury caused by experiment is to retard the process of restoration so that a longer time must elapse after a contraction has occurred. He finds, however, and the fact is of great importance, that nervous action can remove a partial block, and that it does so because it expedites the recovery of the conduction power of the muscle. One of the most important results of this valuable contribution of Gaskell is to show that by nervous influences there may be increase or diminution of the five different aspects of cardiac activity which he analysed—rhythmicity, excitability, conductivity, contractility, and tonicity.

The chief criticism to which the observations and deductions of Gaskell are open lies in the fact that there is in every case the presence of nerve tissue. Further, the changes in rhythmicity and the other functions which he describes as the result of experiments on the vagus, seem to me strong arguments for a nervous origin of these functions.

In one of his interesting contributions, Carlson points out that we know nothing of any action of the heart in the absence of, or apart from, motor and augmentor nerves. It is certainly true that no drug abolishes the action of these nerves without producing some damage to the heart muscle, and therefore experimentation on the vertebrate heart involves, not merely the heart muscle, but the motor and augmentor nerves. He further contends that there is as yet no proof that the vagi act directly on the heart muscle, and that it is as easy to explain the results of experiments on these nerves by means of the neurogenetic as of the myogenetic theory. He holds that Gaskell's researches and observations do not prove such a direct action, and he does not believe that Porter is right in regarding his own experiments as proving the myogenetic view.

The long series of papers produced by Engelmann upon the properties of cardiac muscle may be regarded as containing the most exhaustive statement of the myogenetic theory, and the oration which he delivered in December, 1903, may be accepted as the concluding summary, up to the present date, of his views. In this eloquent and interesting address he points out that the most important difference between the two explanations of the cardiac movements lies in the entirely different interpretation of the ganglionic system of the heart. Both hypotheses equally acknowledge that the source of the stimulus and the mechanism of co-ordination lie in the heart itself. He recalls how the analogy of the automatic and rhythmic stimuli by nerve centres of co-ordinated muscular movements, as in the respiration and the digestion, furnished a hypothesis for the movements of the heart which gradually become a dogma, and, for many, even an axiom. He shows that the first shock which the neurogenetic theory received came from observations upon the ureter, which can be observed in the total absence of ganglion cells to manifest spontaneous peristalsis, and even shows something like the refractory phase seen in cardiac activity. But it seems to me that in this statement sufficient account is not made of its nervous structures. Engelmann states that stimulation of the efferent nerves fails to produce contractions of the ureter, while irritation of the muscular wall excites contraction. But in this statement there is no proof, As is well known, the ureter is abundantly supplied with nerves and in cases of obstruction the contractions of its walls are

experienced in the form of severe pain. Who can prove that the movements caused by direct irritation are not the result of stimulation of the nerves contained in the walls? There remains the statement that stimulation of the nerves coming to the ureter fails to produce contractions. Before finally accepting this assertion, the experiments will require once more to be repeated.

In the next place, Engelmann points out that the possibility of independent periodic contractions is not entirely confined to those parts of the heart which contain ganglion cells, and he therefore assumes that these structures are not necessary for the production of rhythmical contractions. As is, however, now universally recognised, ganglion cells are scattered over every part of the heart, and, inasmuch as the property of spontaneous contraction is directly proportional to the number of these ganglion cells, the force of the argument seems to me to lie otherwise than is put by Engelmann and the rest of the myogenesists. It has further been proved by Berkeley, Morison, and others, that innumerable nerve cells interlace with the muscle cells in every part of the heart. This fact is admitted even by the most ardent upholders of the myogenetic theory, and they allow that it is difficult to advance any convincing proof of their views in consequence of the close connection between muscle cell and nerve fibre. Kronecker, who has consistently opposed the myogenetic conception, very ably discusses this aspect of the question in his Hamburg address, and we know that Dogiel, Apáthy, Bethe, and Nissl attribute very important functions to nerve fibres. Bearing upon this particular aspect of the subject, it may be stated at this point that Wenekebach, who is one of the stoutest upholders of the views of Gaskell and Engelmann, is driven to state that it is, in itself, more probable that an important function like the production of the stimulus to contraction, which is maintained for a considerable time in an excised portion of the heart wall, should have its origin in the intact muscle cells than in the separated nerve fibres. This argument has absolutely no weight; we shall see afterwards that the nervous textures of the heart retain their vitality long after the heart muscle has become absolutely functionless, when both are equally subjected to destructive influences.

The arguments from embryology, based particularly on the researches of the younger His, are powerfully stated by Engelmann.

It is acknowledged on every hand that in the development of the chicken the heart begins to show movements as early as the second day, whilst the first appearance of the cardiac ganglia takes place on the sixth, and that, according to Pflüger, the human embryo shows periodic movements of the heart in the third week, while ganglion cells are only developed in the fourth. Engelmann pertinently asks, Why should neurogenetic automatism be necessary in the later periods of development, when it is unnecessary in the earlier? In other words, Why should the cause of the heart-beat be different after the entrance of the cardiac ganglia to what it was before?

It cannot be gainsaid that these embryological considerations constitute the most important of all the arguments in favour of myogenesis. The heart of the embryo certainly beats before any specialised nervous tissue can be discovered in connection with it, but it must also be remembered that it beats before any distinctive muscular structure can be demonstrated in it. The argument has, therefore, been pushed too far, and although the facts absolutely prove that the functions of the embryonic heart are automatic, they do not prove that these functions are more myogenetic in origin than the movements, for example, of an *amœba*. In Wenckebach's remarks upon the subject he mentions that phylogenetically the muscle cell has developed from a less differentiated structure with nervous and muscular properties, and recalls that, in the lower animals, nervous impulses and contractile processes are united in the same cell. It is difficult, indeed, to see how such facts can be construed as arguments in favour of the myogenetic theory.

Engelmann further lays stress upon the observations of Biedermann, that ordinary voluntary striped muscle fibres in the fully grown frog may be caused to show periodic twitchings in salt solutions after every nervous influence has been shut off by means of curara. But how far the effect of curara upon the different nervous tissues has gone in such experiments has yet to be proved. These various considerations have led Engelmann to the conclusion that the source of the automatic stimulus of the heart is to be placed in the muscle cells, and not in the cardiac ganglia. Recognising the muscular tissue of the sinus as the site of origin of normal stimuli, he asks the further question, whether these stimuli arise everywhere in it or only in a restricted spot? He holds it a matter of much importance, as now determined by recent

researches, that the sinus is possessed in all its parts of the power of producing automatic stimuli, although not to the same degree in every region. In this we shall see he is in opposition to the facts demonstrated by Hering. Dealing with the mode of origin of motor impulses in the muscular tissue, Engelmann holds that for the followers of the neurogenetic theory there are two possibilities. Either the intracardiac motor ganglion cells are automatically active, or they are secondary to external influences, whether through the blood or the lymph, on the one hand, or through intracardiac reflexes by means of cellulipetal nerves. For the upholders of the myogenetic theory who do not recognise the existence of intracardiac musculo-motor nerve centres, the reflex hypothesis falls to the ground. What, then, are the external influences operative here? Is it the blood stream which, from the days of Haller to those of Goltz, has for many physiologists been the sole stimulus? This is impossible, as the heart beats long after every trace of blood or other nutrient fluid is allowed to approach it. The influence of the lymph between the muscle fibres is also, for similar reasons, rejected. The only recognised stimulus to contraction is that produced within the muscular elements through tissue changes, in which connection Engelmann cites the investigations of Howell and Loeb upon the reactions of the various ions and the tissues.

The co-ordination of the cardiac movements and the conduction of the motor impulses is attributed by Engelmann to the muscular connections which have in recent years been described; and, to get over the difficulty of the almost instantaneous conduction of impulses through the auricles and through the ventricles, while a comparatively long time elapses between their respective contractions, Engelmann ascribes with Gaskell a more restricted and embryonic power of conduction of motor stimuli to the muscular bridges. He believes the facts of artificial stimulation in different parts of the heart show that the conduction may be reversed, and he regards this as being highly antagonistic to any theory based upon nerve conduction. Again, he points to the rapidity with which motor impulses pass through the heart, which is much less than in the ordinary motor and sensory nerves. From all these facts he holds that the theory of neurogenetic conduction and co-ordination is no longer tenable, and he therefore concludes as follows:—

“So stellt sich uns denn das Herz dar als ein Muskel, der ohne Mitwirkung von Nerven und Ganglien nicht nur sich selbst erregt, sondern der auch die Succession und Koordination der Bewegungen seiner einzelnen Abteilungen ohne Mithilfe intracardialer Nerven-elemente in zweckmässiger, die peristaltische Fortbewegung des Blutes veranlassender Weise auf rein myogenem Wege zustande bringt.”

Engelmann goes on to claim the law of maximal contraction, enunciated by Bowditch, as an argument in favour of myogenesis, and to appropriate the refractory period, discovered by Marey, as a further proof. Here, however, to the philosophic mind, both these phenomena are as easily explained by the one theory as the other. With regard to the relationship of the nerves and the cardiac functions, he does not agree with Hensen in his interpretation of his careful microscopic observations, yet he waxes somewhat angry over the charge sometimes brought against the myogenetic theory, that it takes no account of the influence of the nervous system, and particularly of the nerves of the heart. He claims that the theory throws unexpected light upon the rôles of these nerves, and proceeds to say :—

“Freilich—und dies muss als Grundlage aller heutigen Anschauungen und aller weiteren Betrachtungen über die Innervation des Herzens festgehalten werden—motorische Ganglienzellen und motorische Nervenfasern im gewöhnlichen Sinne des Wortes besitzt, wie wir oben sahen, das Herz nicht, weder in seiner Wand, noch ausserhalb. Die Ganglien und Nerven werden somit nur, and die Erfahrung bestätigt das, die selbständige Tätigkeit der Herzmuskeln zu modifizieren, zu heben oder zu hemmen, instande sein. Aber auch hiermit bleibt, wie wir alsbald näher sehen werden, den Herznerven eine reiche Fülle wichtiger Aufgaben zuerteilt.”

In his final description of the influence of these nerves, one cannot but be struck by the fact that he is in antagonism to other distinguished adherents of the same school, since he, in stating the functions of the intracardiac ganglion cells, expresses the view that they are mainly inhibitory, whereas His and Romberg say, “Die Herzganglien sind rein sensibel.” In other words, the opinions of some of the myogenetic leaders cancel each other. The idea has more than once occurred to my mind that certain of the more

ardent myogenesisists feel themselves in much the same case as some of the rigidly orthodox in theology when face to face with the early discoveries of geology. It may be remembered that when put hard to it to explain the presence of ever higher forms of life in the newer strata, these disputants expressed the notion that the devil had placed the fossils in the rocks to be a snare for the children of men.

The arguments derived from the recent studies of the connections between the vein and the auricle, as well as those between the auricle and the ventricle, together with the wonderful ramifications of the Purkinje fibres, which we owe to the indefatigable researches of Gaskell, Kent, His, Ewald, Retzer, Braemig, Tawara, and Keith, as well as the experimental researches upon the auriculo-ventricular bundle by His, Humblet, Erlanger, von Tabora, and Erlanger and Hirschfelder, have often been claimed as strong evidence in favour of the myogenetic theory. The same is true of the striking features of heart-block studied from the clinical point of view by a great army of physicians, and of the pathological investigation of morbid changes in the auriculo-ventricular bundle which have been described by Stengel, myself, Schmoll, Jellick Cooper and Ophüls, and Keith and Millar. But it has to be remembered that even the auriculo-ventricular bundle contains not only nerve fibres, but ganglia as well, as has been shown by Tchermak, Tawara, and Keith. That the conduction is by muscle cannot as yet be held as proved. Indeed, the interesting facts that stimulation of the vagus has an effect upon the conductivity of the auriculo-ventricular bundle, as observed by Knoll after the administration of helleborein, and by Cushing and Mackenzie after the employment of digitalin, seems to my mind an argument pointing all the other way. The further observation that the act of deglutition in a patient with impaired conductivity may produce a complete block, as seen by Mackenzie, appears also to me as a strong point in favour of neurogenesis.

It is universally recognised that the seat of the causes of the rhythmic movements lies in the great veins entering the auricular sinus. From the days of Albrecht von Haller to the times of Lauder Brunton, MacWilliam, Engelmann, Hering, Krehl, and Romberg, this fact has been received with general acceptance. But to what particular tissues is the function to be assigned? In one of the most beautiful researches of recent years, Keith

and Flack have attempted to answer this question. They describe the musculature of the sinus as being freely continuous with that of the auricular canal and auricle, and in their search for a well-differentiated system of fibres within the sinus, which might serve as a basis for the inception of the cardiac rhythm, they have been led to attach importance to a peculiar musculature surrounding the artery or arterial circle at the sino-auricular junction. The structure is described as being like that of the auriculo-ventricular bundle, consisting of an intimate network of pale undifferentiated fibres with well-marked nuclei. It is to be observed that Keith and Flack describe the presence of nerve-cells and nerve-fibres, and state that, "although the mass by its connections is undoubtedly muscular the nerves in the neighbourhood of the vena cava appear to come into very intimate connection with it, so that we feel justified in stating a highly differentiated neuro-muscular junction occurs at this point."

The occurrence of a block at the sinus, if the interpretation furnished by Hering and Wenckebach, as well as by Ritchie and myself, is correct, seems to me strongly in favour of neurogenetic conduction. The muscle fibres are certainly not so much restricted as in the case of the auriculo-ventricular bundle, according to Keith, and the occurrence of a block at this point is, therefore, more likely to be the result of disturbed nerve influence than of diminished muscular conductivity. This, in fact, is fully recognised by Keith and Flack in the contribution just referred to, which appeared after these remarks had been written. They frankly acknowledge that a sino-auricular block cannot be due to any anatomical lesion of a narrow bridge of fibres, but must arise from the depression, probably of vagal origin, of the muscular tissue. We may well ask, why muscular tissue?

The occurrence of irregularity of the heart in early life seems to me to have an important bearing upon this subject. The long series of careful observations made by Mackenzie have led him to the conclusion that the irregularity of early life is commonly of nervous origin, and his conclusions entirely commend themselves to my judgment. This view necessarily leads to the probability that interference with the heart functions arising in such a way is more likely to be produced through disturbances of the intracardiac nervous system than of the muscular tissues. The irregularities of later life are undoubtedly produced very commonly by structural

alterations in the muscular as well as in the nervous tissues, and no argument from them can be deduced; but many of the toxic forms of arrhythmia in patients suffering from gouty troubles are, like early irregularity, to be regarded as in favour of the neuro-genetic theory.

The action of chemical substances has sometimes been invoked as an argument in favour of the myogenetic theory. It was shown by Biedermann more than 25 years ago, that the skeletal muscles may show rhythmical contractions under the influence of alterations in the chemical composition of the fluid by which they are surrounded, and more recently Howell and Loeb have demonstrated that certain ions have the faculty of producing such phenomena. Here again, however, it is a mere assumption that such agents act on the purely muscular protoplasm. Seeing that the muscle cell is inextricably interwoven with nerve fibres, and that these nerve fibres, as Carlson has shown, are less subject to destructive changes than the muscle cell, the argument would seem to the unbiassed mind to lie in an entirely opposite direction.

The observations of Magnus and of Sollmann are of considerable importance in their bearing upon the question at issue. They have been able to prove that distension of the coronary arteries is able to start and to maintain the beat of the heart. It seems probable that Sollmann is correct in his conclusions that this fact is in favour of the neurogenetic theory, since it seems likely that the effect of distension is to stimulate the nerves in the walls of the vessels, whence the impulses are conveyed to the ganglia.

It is often stated that the rate of conduction is too slow to be produced by nerve agency; but Carlson has shown that in the intrinsic heart nerves of the king-crab conduction is eight or ten times less than in the peripheral motor nerves. Fully realising that conduction occurs by the auriculo-ventricular band, Carlson will not allow it to be held as proved that the conduction occurs either by muscular or Purkinje fibres. Gaskell's experiments, which showed that the rate of conduction was altered by the action of the extrinsic cardiac nerves, demand necessarily the existence of nervous tissues in the band. Such nervous tissues have been described by Tchermak, Tawara, and Keith, as has already been mentioned.

The analogy between the movements of the heart and of the peristalsis of the intestines has often been urged as a strong

argument in favour of the myogenetic theory, on the assumption that the peristalsis is due purely to muscular action. Unfortunately for the views of those who have used this argument, the recent researches of Bayliss and Starling, as well as of Magnus, show that the peristaltic movement of the intestines is due to the plexus of Auerbach. Magnus, indeed, has shown that the wall of the intestine of the cat is refractory at the beginning of automatic contraction, but that this only occurs when the plexus of Auerbach is intact. It is to be remembered that Schultz has not been able to confirm this observation of Magnus, and therefore, before accepting it as having an absolute value, we must wait for some further researches. One most interesting fact has recently been ascertained regarding the peristalsis of the intestine in the embryo by Yanase, who has discovered that this function does not make its appearance until the development of the earliest nervous elements. Yanase concludes from his observations that the automatic movements of the foetal intestine are neurogenetic in origin. There are undoubtedly some differences between the state of matters here and in the case of the embryonic heart, in so far as the heart beats before any nervous structures are apparent in it, while the first movements of the intestines are synchronous with the earliest development of nervous structures. The facts investigated by Yanase are, nevertheless, a powerful argument in favour of the neurogenesis of cardiac pulsations.

So far we have devoted attention to the observations and opinions in favour of the myogenetic hypothesis. It is time to turn for a space to facts and views which have been recently advanced in support of the theory of Volkmann.

Observations upon invertebrates, even of lowly types, have been of great assistance in the elucidation of the problems connected with cardiac movements. A very large number of researches have been carried out in this field, of which it is only possible to refer to a limited number, from which most important information has been obtained. Romanes, in his famous Croonian Lecture, showed that in the naked-eyed Medusæ, such as *Sarsia*, excision of the extreme margin of the nectocalyx produced an immediate, total, and permanent paralysis of the entire organ; while in the covered-eyed Medusæ, such as *Aurelia*, excision of the margin of the gonocalyx brought about the same results. The exact nature of the structures contained in the margin of the nectocalyx and of the gonocalyx

was left uncertain by the researches embodied in this contribution of Romanes, but the gap in our information was filled by the investigations of Schäfer. It is important to observe, even so low down in the metazoic scale as the Medusæ, that the textures which in the higher animals are generally looked upon as the most highly differentiated, should have already attained a degree of structural complexity and of functional activity scarcely inferior in many respects to the nervous and muscular tissues of the vertebrata. In a most interesting paper, Schäfer gives a clear demonstration of ganglion cells and nerve-fibres in the margins of the nectocalyx and of the gonocalyx of the Medusæ.

The valuable researches of Carlson upon the invertebrate heart have thrown a vivid side-light upon the relationship of nerve ganglia and heart muscle. In the king-crab the heart is brought into relation with the central nervous system by means of a median nerve cord, containing ganglia, which is connected with the heart by an arrangement of lateral nerves. Carlson finds that section of the nerve cord produces an independent rhythm of the two ends of the heart, and that removal of the nerve cord causes a standstill of the whole organ. The obvious conclusions drawn from these observations are that the heart-beat in *Limulus* is of purely nervous origin, arising in impulses sent by this cord, and that the cord is a centre, or series of centres, whose rhythmical activity is the direct cause of the heart rhythm. The analogy to the mechanism of respiration is perfectly obvious.

In further researches upon *Limulus*, Carlson finds that the ganglia are more numerous at the end of the heart corresponding to the venous sinns of the vertebrate, and, further, that these ganglia are arranged much after the plan seen in the vertebrate heart. The ganglion cells, which are dotted over the heart of the vertebrate, are probably like the ganglion cells of the lower respiratory centres in the cord, in respect of being only active in response to impulses from centres of greater automatism. The nerves from the nerve cord to the heart muscle are of the ordinary motor type in *Limulus*, and stimulation of these produces continuous super-maximal or tetanic contractions. Carlson quotes the observations of Stewart in this connection, that stimulation of the sympathetic nerve causes the heart of the frog to beat after it has been brought into the condition of heat standstill. The nerve cord in *Limulus* can act as a reflex centre, and Carlson finds that the lateral nerve, when separated and

stimulated, gives rise to increased strength of the pulsations, or produces pulsations when the heart is quiescent. In these observations there is reflex augmentation of the pulsating heart, as well as reflex contraction of the heart when at rest. Are these phenomena to be regarded as merely axon-reflexes? Carlson regards this as unlikely, for the change in rhythm involves every part of the heart whose nerve connections are not severed, while, if they were really axon-reflexes, every muscle cell would require to have an axis cylinder process from every motor neuron, which is hardly to be credited. A rise of pressure in the heart of *Limulus* produces effects only when the nerve cord is intact. It has been stated by Engelmann that a contraction of the quiescent heart muscle on stimulation of any extrinsic or intrinsic nerve would be fatal to the myogenetic theory. The facts advanced by Carlson seem to give food for reflection in this connection.

After fully describing the course of action of the inhibitory and augmentor nerves in the king-crab, Carlson shows that the effects of experiment are similar to those seen in vertebrates. The effect of stimulation of the heart after inhibition is the same as after removal of the nerve cord, and therefore complete inhibition is equivalent to throwing the nerve cord out of action.

The obvious criticism of these interesting researches of Carlson, and indeed of all similar investigations on the invertebrata, is that the invertebrate type of heart cannot be regarded as homologous to that of the vertebrates. The organs undoubtedly differ widely in structure, and exact comparison is therefore impossible; it is, nevertheless, a striking fact that Carlson finds so many points of resemblance in the two types. It may be recalled, moreover, that Wenckebach admits there is no fundamental difference between striped and smooth muscle fibres, or between vertebrate and invertebrate muscle cells.

The investigations of Greene upon the physiology of the Californian hagfish, *Polistotrema*, are decidedly suggestive, and, in particular, his observations upon the caudal heart of the animal are of much value. By these investigations he has been able to prove that the rhythmic contractions of the caudal heart are produced by rhythmic discharges of motor impulses which proceed from an automatic caudal heart centre in the spinal cord. To this and similar researches there is always the obvious objection that the organ investigated is not homologous to the mammalian heart.

Freely admitting this, the analogy is a far better one than that furnished by a pianola or a horseman!

It has been asserted that in certain of the invertebrate hearts ganglion cells do not exist, and the cardiac arrangements of *Aplysia* have, in recent years, been often pointed to as proofs of this contention. But more recent investigations have shown that the statements of Straub are not based on solid facts, and we may safely conclude that we do not know anything about the properties of the heart muscle apart from intrinsic nervous tissue and ganglion cells. Schwartz has seen numerous cells along the nerve fibres and vessels of the ventricle, but expresses a doubt as to their nervous nature, from the fact that they possess no nucleated envelopes. As is very well known, the cells in the plexuses of Auerbach and Meissner, where the nature of the cells is undoubted, possess no nucleated envelopes.

In a valuable paper on the volume curve of the ventricles of the mammalian heart, Vandell Henderson applies his results to the elucidation of the properties of cardiac muscle, the functions of the nerve net, and the nature of vagus influence. He is constrained to express his opinion that the behaviour of the mammalian heart is not so easily explained by the ever-increasing complexity of the myogenetic, as by the simpler principles embodied in the neurogenetic hypothesis. He holds that the distinction between the two hypotheses lies in the acceptance or rejection of the idea that the processes which generate the stimulus are distinct from those which react to it, as well as in the acceptance or rejection of the view that the influence of the vagus is not primarily exerted on cardiac muscle, but on the stimulating mechanism contained in the cardiac plexus. He regards the reduced rate of the heart-beat as a lengthening of the periods between the stimuli, and standstill as a phase during which the muscle fibres receive no stimuli; in urging which he gives good reasons for rejecting the views of Stephani, Gaskell, and Engelmann. That the vagus actively causes an increase in cardiac volume, as asserted by Stephani, he disproves. That the vagus promotes anabolic processes, as urged by Gaskell, he shows to be improbable, for the ventricle behaves exactly as the gastrocnemius does when the stimuli are instantaneous and maximal—all depends in both cases on the rate at which stimuli are applied. He further rejects the view of Gaskell that the vagus acts directly

upon muscle, modifying the five functions he has described, and also the still more complex hypothesis of Engelmann, that the vagus has different sets of fibres for the different functions, chronotropic, bathmotropic, dromotropic, and inotropic, which that observer ascribes to the heart of the frog.

Henderson finds from his own experiments that the volume curves obtained from the mammalian heart also show changes in rhythmicity, conductivity, excitability, contractility, and tonicity. He strongly urges, however, that these phenomena are easily explained on the neurogenetic hypothesis, if we only claim for the heart such properties as are possessed by a striped muscle. The processes in the nerve net result in discharges of stimuli into the muscle, similar to those which in the case of ordinary muscle produce similar behaviour. Hence we may infer the properties of the cardiac plexus. The first conclusion to which this line of reasoning leads him is that the plexus normally discharges only maximal stimuli, for every contraction is maximal; and since tonus at every instant is proportional to the number of beats in the period immediately preceding, there must be an entire absence of those subminimal stimuli which induce tone in a resting skeletal muscle. The statement that the plexus of the mammalian heart normally discharges only maximal stimuli, does not mean that the plexus is essentially incapable of submaximal discharges. On the contrary, when the mammalian heart ceases to beat vigorously with complete co-ordination and uniform rhythm, its volume curve may exhibit a wide diversity of forms. Such curves resemble the contraction curves of striated muscle induced by stimuli of irregular series and submaximal strength, and may be explained accordingly as due to irregular and submaximal discharges by the cardiac plexus. Regarded thus they strengthen the view that cardiac muscle is merely a somewhat modified variety of striated muscle, and that the behaviour of each is equally the expression of the stimuli discharged into its fibres through nervous channels. The essential difference in the behaviour of the heart and that of a skeletal muscle in the living body lies in this—that the contractions of the latter usually occur under the influence of a very rapid series of submaximal stimuli. The beat of the heart, on the contrary, is induced by a single and nearly instantaneous stimulation.

“To the cardiac plexus,” Henderson says, “we must accordingly

assign the property of effecting a continual algebraic summation of various stimuli, chemical (such as oxygen, the Na, K, and Ca ions, etc.), mechanical (from the coronary and venous pressures), and nervous (from vagi and accelerators), in such a manner that the excited state of each unit of the plexus is not discharged into the muscle until it has swollen to the proportion of a maximal stimulus. Indeed, by utilising the modern view of the properties of the synapse, we may explain the all or none character of the heart-beat by assuming that, as compared with the interneuronic connections in the central nervous system, the junctions of the nerve units composing the cardiac plexus are of high resistance. Normally they yield no passage to any excitation of an intensity less than that which will induce a maximal contraction in the cardiac muscle. When, however, the pressure of excitation becomes sufficient to break through the junction, the passage is wholly free and complete.

“Furthermore, the entire range of vagus influence appears to be explainable on this view by the assumption that all its fibres belong to a single class, and that their function is to increase, or under uniform normal conditions to assist in maintaining, the resistance of these junctions. This assumption accounts for the immediate results of the section of both vagi previously described. It accounts for the slowing of a normal rhythm without increase of amplitude of beat; for while under such conditions the excitations must be dammed back to a supermaximal intensity, supermaximal stimuli can induce in muscle only maximal contraction. It accounts for the increased amplitude which accompanies slowing, when the functional activity of the plexus is below normal and its discharges are therefore submaximal. Finally, it accounts for the variations induced by vagus stimulation in rhythmicity, excitability, and conductivity.”

The phenomena of inhibition by means of the vagus provide matter for consideration. MacWilliam has pointed out that whatever may be taking place in the nerve cells, on vagus inhibition there is a profound change in the muscle. This is shown most decisively in certain hearts in which (as in the eel and the newt) the vagus acts very powerfully. In these hearts the cardiac muscle becomes absolutely inexcitable by such direct stimuli as powerful induction shocks and mechanical irritants. These facts are held to show muscular inhibition, for mere inhibition of nerve cells could not

prevent the response of the muscle when directly excited. But what of the nerve fibres?

In a recent contribution, Hering shows that the fact of many contractile parts of the supra-ventricular region of the heart being destitute of automatic properties is not in favour of myogenesis. He further points out that some additional factor must be at work. If we accept a nervous automatism he thinks we shall require some additional hypothesis, that is, if we ascribe automatism to nerve fibres, since they are found everywhere. But in the case of the ganglion cells the matter stands differently, as they vary in their distribution, and he points out from his experiments, compared with the researches of Krehl and Romberg, that those parts which he found destitute of automatism have no trace of ganglion cells. He shows that some of the difficulties connected with the neurogenetic theory are met by the fact that there are different kinds of ganglion cells with various functions, which cannot be urged of muscle cells.

An important argument against myogenesis is to be derived from the fact that the heart may conduct impulses without manifesting contraction. Fredericq observed that the apex of the heart might be electro-negative to the base, or, in other words, that it contracted before the base. Waller and Reid found that the apex may either precede or follow the base in the manifestation of electro-negativity. Bayliss and Starling, on the other hand, found that in health the base always manifested electro-negative conditions before the apex, but that in hearts which had been damaged the apex might precede the base. Some light upon this subject has been thrown by the researches of Carlson on *Limulus*. He finds that the heart walls may conduct impulses without showing contraction. After soaking the heart until the condition of water-rigor appears, it is clear that the nerves can withstand the evil effects of the process better than the muscle cells, and, after inducing that condition in *Limulus*, he is able to prove that the conduction does not take place by muscle but by nerve. He observes that analogous effects may be produced by heat, and that after its application the muscle fails to respond, while the ganglion cells are still active.

Amongst the opponents of the myogenetic theory, von Cyon stands prominently forward as one of the most formidable in destructive criticism. In his famous paper, "Myogen oder Neurogen," he furnishes one of the most acute examples of physio-

logical polemics which our generation has witnessed. To this has more recently been added his work on the nerves of the heart, which also abounds in trenchant criticism. On this occasion it is impossible to follow the author through his analysis of the myogenetic hypothesis, but it may be said in a word that his opinion is strongly in favour of the views of Volkmann and his followers.

My pleasant duty is nearly accomplished. Will you permit me to express the hope that the lengthy examination of the doctrines necessary for their clear apprehension has not been intolerably wearisome? When turning the subject over in my thoughts lately for the purpose of addressing you this evening, the quaint remarks of Burton on excessive mental effort as a cause of melancholy recurred to my mind. "No labour in the world," he says, "like unto study."

The conclusion of the whole matter, so far as can be seen at present, lies in a question of probabilities. Five years ago my adhesion was almost given to the myogenetic hypothesis, but much clinical observation and considerable pathological investigation, as well as laborious study and critical analysis of all the important contributions upon the subject, have led me to the conclusion that the view of Volkmann still furnishes a nearer approach to a satisfactory explanation of the facts than any other which has since been advanced. In the remarks which have been made, a running commentary upon the various views has been offered in connection with each of them, and it has been my earnest effort, in doing this, to remain as free from personal predilection as is possible for ordinary human nature.

To summarise the arguments, let me state succinctly the various points which have been under review. The embryological facts cannot be claimed by the adherents either of myogenesis or of neurogenesis, for the heart begins to beat before muscle or nerve appears. The anatomical conditions do not favour one or other hypothesis, for nerve and muscle are closely interwoven in the region where the pulsation is initiated. The physiological evidence is equally claimed by the upholders of both views, and structural considerations show that both have much weight on their respective sides. The pathological results are equally impartial in their bearing, and prove neither opinion. The clinical observations, however, are distinctly easier to explain on a neurogenetic basis. Beyond all doubt, the singular structure recently described by

Keith and Flack is the mechanism by means of which pulsation is initiated, but the original impulse, to my mind, is clearly given by the nervous elements.

Dealing with matters of such intricacy and complexity, it must be frankly confessed that such proof as will satisfy the demands of a rational scepticism is still far from attainment. It is, indeed, difficult to see at the present moment whence such evidence is to be obtained. Out of the patient investigations and indefatigable researches of so many observers it is to be hoped that a means of arriving at the truth must come at last. Meantime, as has been already said, the whole matter is a question of probabilities. In default of absolute proof we must be guided by the weight of evidence and by the inherent acceptability of any explanation. The simplicity of the neurogenetic as compared with the complexity of the myogenetic hypothesis pleads eloquently for the former. Any view invoking the necessity of a dual control must necessarily be less worthy of adoption than another demanding only a single agency; as Newton says: "*Natura enim simplex est, et rerum causis superfluis non luxuriat.*" "That man is always happy," says Ruskin, "who is in the presence of something which he cannot know to the full, which he is going on to know." In the conflicting statements and discordant opinions arising out of the consideration of this central point of circulatory physiology, we assuredly ought to be happy!

"*Causa latet, vis est notissima fontis*" seems to me singularly applicable to the points at issue, and, reviewing the whole circumstances, many of us will probably be inclined to agree with our late Laureate that, as regards the subject under discussion,

"We have but faith: we cannot know;
For knowledge is of things we see."

